

The Congenital and Acquired Solitary Kidney

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The embryonic insult that results in unilateral renal agenesis may involve not only the ureteral bud but also other mesonephric duct derivatives, including the seminal vesicles, vas deferens, and epididymis; in the female with a solitary kidney, müllerian duct anomalies frequently occur. Normal renal development depends upon a normal ureteral bud, which undergoes orderly branching and penetrates the metanephric blastema at about the fifth week of gestation. Ureteral and kidney development are thought to be interdependent, and when there is failure of the ureteral bud to form or absence of the nephrogenic ridge, the kidney does not develop normally. Unilateral renal agenesis is compatible with normal longevity and does not predispose the contralateral kidney to greater-than-normal risk; nevertheless, patients should have annual surveillance, including a blood pressure measurement, serum creatinine if not initially normal, and urinalysis to detect proteinuria. Removal of one kidney leads to structural and functional changes by the remaining kidney, including increased filtration of the remaining glomeruli. These functional changes have generally been considered beneficial because they mitigate the reduction in the total glomerular filtration rate that would otherwise occur, but experimental evidence suggests that these changes may have an adverse effect on the remaining kidney. Clinical evidence shows that these changes do not lead to renal deterioration in kidney donors because the renal function of kidney donors is well preserved in over 20 years of follow-up after donor nephrectomy.

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Normal renal development depends upon a normal ureteral bud, which undergoes orderly branching and penetrates the metanephric blastema at about the fifth week of gestation.¹ Induction of ureteral bud branching depends on the presence of a normal metanephric blastema.² When there is failure of the ureteral bud to form or absence of the nephrogenic ridge, the kidney does not develop normally. Ureter development and kidney development are

thought to be interdependent. Autopsy studies reveal that renal agenesis can occur with the development of either a partial or a completely normal

lead to URA and abnormal mesonephric duct development. The specific timing of this insult affects the crossover of the müllerian ducts

screening, it has been found that multicystic dysplastic kidneys (MCDK) involute before birth. These may account for some of the cases that were previously thought to be URA.⁹

Ureter development and kidney development are thought to be interdependent.

ureter, and a rudimentary kidney can be present in some cases where there is no identifiable ureter.³

The embryonic insult that results in unilateral renal agenesis (URA) may involve not only the ureteral bud but also other mesonephric duct derivatives, including the seminal vesicles, vas deferens, and epididymis.^{4,5} In the female, the müllerian duct derivative is dependent upon the normal development of the mesonephric duct; therefore müllerian duct anomalies occur frequently in URA.⁶ An embryological classification has been proposed based upon the timing of the insult (Figure 1).⁷ Type I anomalies occur before the fourth week; there is absence of the mesonephric and müllerian duct derivatives, resulting in a solitary kidney and unicornate uterus (Figure 1A). Type II anomalies occur early in the fourth week and

and their subsequent fusion (Figure 1B). These patients have a solitary kidney and a didelphic uterus with obstruction of the ipsilateral horn and vagina. Type III anomalies occur after the fourth week and result in only URA.

Incidence

The incidence of URA is unknown because it is usually asymptomatic. Autopsy studies report an occurrence of about 1 in 1000.⁸ The incidence of

Associated Anomalies

The ipsilateral ureter is absent in 50% of cases, and contralateral vesicoureteral reflux is found in about 30%.^{3,10,11} There can be varying degrees of hydronephrosis and hydroureteronephrosis in the solitary kidney.^{10,11} URA is commonly associated with genital anomalies, which are 3–4 times more frequent in females than in males.¹² In both sexes the gonads are usually normal, but the structures that derive from the wolffian and müllerian ducts can be anomalous.¹ Uterine anomalies occur in 1 in over 500 females, and 43% of those have URA¹²; 30% with URA have reproductive tract anomalies.⁶

These patients have a solitary kidney and a didelphic uterus with obstruction of the ipsilateral horn and vagina.

symptomatic URA is about 1 in 1500.⁴ The male-to-female ratio is 1.8 to 1, and it occurs more frequently on the left.^{1,4} With the advent of prenatal

The most common female reproductive tract anomalies include a true unicornate uterus, with complete absence of the ipsilateral horn and

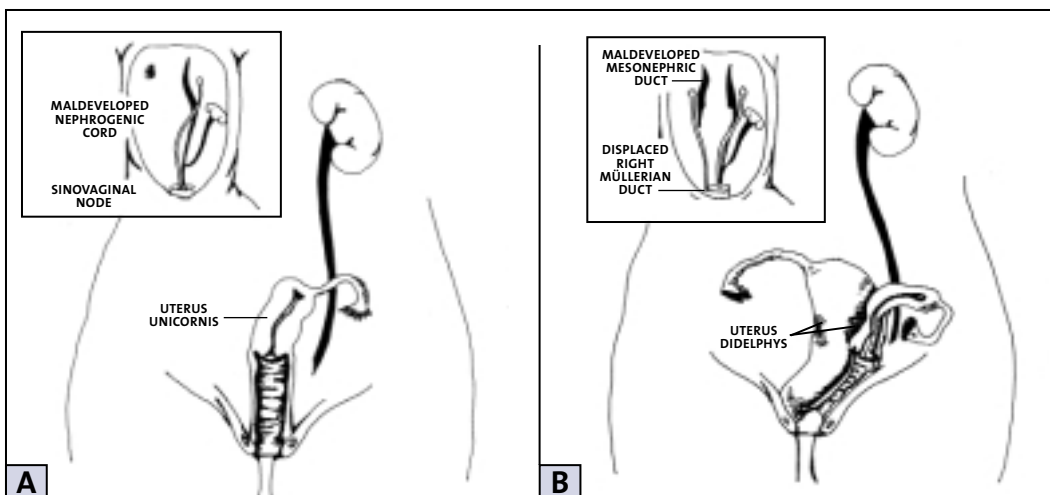


Figure 1. Type I anomalies occur before the fourth week and result in a solitary kidney and unicornate uterus. Type II anomalies occur early in the fourth week and result in a solitary kidney and a didelphys uterus with obstruction of the ipsilateral horn and vagina. (A) Solitary kidney and unicornate uterus. (B) Solitary kidney and didelphys uterus with obstruction of the ipsilateral horn and vagina. Reproduced from Magee MC, Lucey DT, Fried FA. A new embryologic classification for uro-gynecologic malformations: the syndromes of mesonephric duct induced müllerian deformities. J Urol. 1979;121:265–267, with permission of the publisher.

fallopian tube, and a bicornate uterus with rudimentary development of the horn on the affected side.¹³ An obstructed hemivagina and uterus didelphys (double uterus due to incomplete midline fusion of müllerian ducts) are also often present. Because clinical presentation includes lower abdominal pain or a pelvic mass in a pubertal female, the diagnosis of hematometocolpos is usually not considered.¹⁴⁻¹⁶

URA can be associated with the Mayer-Rokitansky-Küster-Hauser syndrome, in which there is congenital absence of the uterus and vagina.¹⁷

The structures that derive from the wolffian and müllerian ducts can be anomalous.

Typically, there are bilateral symmetrical rudimentary uterine anlagen and complete absence of the vagina, with normal fallopian tubes and ovaries. In the atypical form, there are asymmetric uterine remnants, abnormal fallopian tubes, and cystic or anomalous ovaries. The ovarian and renal anomalies are almost always associated with the atypical form.¹⁸

In males, anomalies of reproductive organs occur in only 20% of patients with URA.^{4,6} These include absence or atresia of the seminal vesicles, vas deferens, and epididymis.¹⁹ When the vas has been found to be absent in adult males, 79% were found to have an absent ipsilateral kidney.⁵ The testes are usually uninvolved, and cryptorchism is rare.¹

Anomalies of other organ systems can be associated with URA, including those of the cardiovascular system (30%) and musculoskeletal system (14%).⁸ Unilateral renal agenesis is found in 30% of patients with the vertebral, imperforate anus, tracheoesophageal, and renal (VATER) syndrome.²⁰ Because the adrenal gland

has a different embryological origin, it is absent in only 10% of cases.³

Radiologic Evaluation

Prenatal sonography has increasingly identified fetuses with URA.¹ Compensatory renal growth has been documented in human fetuses with a solitary functioning kidney.²¹ When the vas or body or tail the epididymis is not palpable or an anomalous vagina or uterus is diagnosed, renal sonography is indicated.¹ Sonography reveals a characteristic flattening of the adrenal gland when the kidney is absent.²² A plain film of the abdomen

may demonstrate a more medial position of the splenic and hepatic flexures, suggesting true URA, whereas the bowel position is normal when there has been involution of a MCDK simulating the appearance of URA.^{23,24} If URA is diagnosed prenatally, a pelvic sonogram should be performed. If a uterine anomaly is suspected, magnetic resonance imaging is the best modality to delineate the anatomy of the reproductive tract.²⁵ URA is confirmed on technetium 99m-dimercapto succinic acid(99

number of glomeruli as a normal kidney.²⁶ Argueso and colleagues reported on the late effects of congenital URA, including proteinuria (19%), hypertension (47%), and mild renal insufficiency (13%), in middle-aged patients.²⁷ Overall survival was not affected by URA. URA is compatible with normal longevity and does not predispose the contralateral kidney to greater-than-normal risk.

Rugui and coworkers studied a small group of patients with URA and found an increased incidence of hypertension, hyperuricemia, and decreased renal function but no proteinuria.²⁸

Ritchey reviewed 155 patients ages 2-84 years with URA, with mean follow-up of 44 years. Most (79%) had a normal serum creatinine. Only 5 patients had an abnormal elevation in creatinine (above 2.0 mg/dL). Significant proteinuria (2+ or greater) was found in only 8%, and hypertension occurred in 21%.²⁹ In the long term, patients should have annual surveillance, including a blood pressure measurement, serum creatinine (if not initially normal), and urinalysis to detect proteinuria.

Dietary Precautions

There is still controversy about the role of protein restriction for patients with a solitary kidney, especially in

Compensatory renal growth has been documented in human fetuses with solitary or functioning solitary kidneys.

mTc-DMSA) scanning.¹ A voiding cystourethrogram is indicated, because there is a high incidence of vesicoureteral reflux.¹⁰

Long-Term Prognosis

A recent study has shown that the solitary kidney is not hypertrophic but hyperplastic and has twice the

children. Brenner and colleagues reported that excess dietary protein is deleterious to the kidney when there is chronic renal failure.³⁰ Several investigators have shown that dietary restriction may slow the rate of progression of renal deterioration.³¹⁻³³ Although it is reasonable to restrict protein intake in adults with a crea-

tinine clearance less than 50% of normal, protein restriction in children may lead to malnutrition. The appropriate protein intake for children with chronic insufficiency has not been determined. Children with a creatinine clearance of less than 50% of normal may safely limit protein intake to the recommended daily allowance of protein for children.³⁴

Sports Participation

Renal injuries in children are second only to head injuries in frequency,³⁵ and 10% of renal injuries occur in congenitally malformed kidneys.³⁵ Blunt injuries occur in 60%–90% of patients, and only a renal contusion occurs in most cases.³⁶ In the past, the American Medical Association recommended disqualification of athletes with renal disease or solitary kidneys from collision or contact sports.^{37,38} Recently, people with disabilities have won the right to participate in contact sports, citing the Federal Rehabilitation Act of 1973, and athletes who had previously been disqualified from participation in some sports are now able to compete.³⁷

In 2001, the American Academy of Pediatrics (AAP) published an updated statement on medical conditions affecting sports participation.³⁹ The AAP classifies sports by their degree of contact and collision. The AAP does not recommend participation in boxing and suggests only a limited amount of body checking for hockey players of 15 years and younger. Individuals with one kidney need individual assessment for contact/collision and limited-contact sports. Protective equipment such as “flak-jackets” may make limited-contact/impact sports safe.^{37,38} Sports with high contact/collision potential are boxing, basketball, diving, field hockey, football (tackle), ice hockey, lacrosse, martial arts, rodeo, rugby, ski jumping, soccer, team handball,

water polo, and wrestling. This does not mean that some of the limited-contact sports, such as downhill skiing and gymnastics, cannot be as dangerous as high-contact or collision sports.³⁹

The Acquired Solitary Kidney

Renal Function Following Nephrectomy in Children

The removal of one kidney leads to structural and functional changes in the remaining kidney. One of the major functional changes is increased filtration of the remaining glomeruli.⁴⁰ These functional changes have generally been considered beneficial because they mitigate the reduction in the total glomerular filtration rate (GFR) that would otherwise occur after nephrectomy. However, experimental evidence suggests that these function-

failure following subtotal renal ablation is focal glomerulosclerosis. Only three children have been reported to have developed focal segmental glomerulosclerosis many years after completion of treatment for Wilms' tumor.^{44,45} The only patient to develop renal failure also had renal artery stenosis of the solitary kidney and had received abdominal irradiation.⁴⁵

Only limited data exist assessing long-term renal function in children who have undergone nephrectomy and have only a solitary functioning kidney. Argueso and colleagues reported that children with acquired solitary kidneys followed for a mean of 25 years were at increased risk of proteinuria and renal insufficiency, although none had developed end-stage renal disease.⁴⁶ Few studies have assessed long-term renal func-

Most experimental studies involve a loss of over three quarters of the total renal mass, although one study noted abnormalities after removal of only one kidney.

al alterations may have an adverse effect on the remaining kidney.

Laboratory studies in animals have shown that a marked reduction in renal mass leads to progressive sclerosis of the remaining glomeruli, resulting in proteinuria, hypertension, and progressive azotemia. Most experimental studies involve a loss of over three quarters of the total renal mass, although one study noted abnormalities after removal of only one kidney.⁴¹ Most of the experimental studies of hyperfiltration-induced injury have been performed in rats, and it is unclear if these findings are applicable to humans.^{42,43}

The data in humans regarding renal damage from hyperfiltration following nephrectomy are less clear. The renal lesion that occurs in animals and that progresses to renal

tion in children following nephrectomy. The abnormalities identified include microalbuminuria, proteinuria, and a reduced GFR.^{47–50} However, other investigators have found no significant alterations in renal function.^{51–53}

Levitt and colleagues evaluated 53 patients at a mean of 13 years after treatment for Wilms' tumor.⁴⁷ Ten patients (19%) were found to have a decreased GFR ($< 80 \text{ mL/min/1.73m}^2$), 6 (11%) had hypertension, and 5 (9%) had increased urinary excretion of albumin. None of the patients had developed renal failure. Forty of the 53 patients had received radiation (300–1720 cGy) to the remaining kidney. Factors found to be associated with renal dysfunction were age of under 24 months and radiation doses greater than 1200 cGy to the remaining kidney. All 6 patients with radia-

tion nephritis as the etiology for renal failure in this review received radiation doses exceeding 1200 cGy to the remaining kidney. Another report of 27 patients with Wilms' tumor noted that 33% had a creatinine clearance of under 55mL/min/1.73m² but did not state whether any of these patients had proteinuria or other clinical manifestations of renal insufficiency.⁴⁸

Baudoin and colleagues reported on 111 patients, 14 with Wilms' tumor, who underwent nephrectomy in childhood and were followed for up to 50 years.⁴⁹ They found that renal function was well maintained at 75% of the reported normal two-kidney value. After an interval of more than 25 years postnephrectomy, there was a tendency for a gradual increase in urinary protein and albumin excretion and decrease in GFR. However, there were only 3 patients with a GFR below 60/mL/min/1.73m². Robitaille and colleagues evaluated 27 patients (4 had Wilms' tumor) for a mean of 23.3 years after nephrectomy and found only minimal changes in GFR when compared to controls; none had significant pro-

teinuria or hypertension.⁵⁰

Others have assessed the renal functional reserve capacity after unilateral nephrectomy in childhood.^{54,55} These studies evaluate the function of the solitary kidney after oral protein loading. The report by Regazzoni and colleagues⁵⁴ found that renal reserve capacity was normal in the first decade after nephrectomy but decreased by 50% by 10–20 years later and 66% by 20–30 years later.

Investigators with the National Wilms' Tumor Study Group (NWTSG) have retrospectively reviewed the incidence of renal failure following treatment for Wilms' tumor.⁵⁶ Individuals with bilateral tumors had a much higher incidence of renal failure. In patients undergoing nephrectomy for unilateral tumor, they found an incidence of less than 0.26% of 5368 patients reported to NWTSG studies 1–4. Two thirds of the patients with renal failure after unilateral nephrectomy had Denys-Drash syndrome-associated nephropathy.⁵⁶ There were few patients with late onset of progressive renal failure suggestive of hyperfiltration-induced injury.

A more recent paper from the NWTSG identified an increased risk of renal failure in patients with Wilms' tumor and aniridia (WAGR) or genitourinary anomalies who had undergone unilateral nephrectomy.⁵⁷ The cumulative risks of renal failure at 20 years from diagnosis were 38% and 11%, respectively. Of great interest was that the median age at the time of renal failure in the WAGR syndrome was 14.2 years. All cases of renal failure in males with genitourinary anomalies occurred after puberty. These investigators postulated that the late onset of renal failure in patients with genitourinary anomalies and the WAGR syndrome was due to mutation in the *WT1* gene. Patients with the Denys-Drash syndrome usually have a germline mutation of *WT1*. It has been suggested that the severe nephropathy and genital abnormalities in these patients are due to the action of the altered *WT1*. This study suggests a gradation of phenotypes associated with *WT1* mutations. It starts with patients having genitourinary anomalies and a moderate long-term risk of renal

Main Points

- Autopsy studies reveal that renal agenesis can occur with the development of either a partial or a completely normal ureter, and a rudimentary kidney can be present in some cases where there is no identifiable ureter.
- The embryonic insult that results in unilateral renal agenesis (URA) may involve not only the ureteral bud but also other mesonephric duct derivatives, including the seminal vesicles, vas deferens, and epididymis.
- The most common female reproductive tract anomalies include a true unicornate uterus, with complete absence of the ipsilateral horn and fallopian tube, and a bicornate uterus with rudimentary development of the horn on the affected side.
- Anomalies of other organ systems can be associated with URA, including those of the cardiovascular system (30%) and musculoskeletal system (14%).
- The removal of one kidney leads to structural and functional changes in the remaining kidney, including increased filtration of the remaining glomeruli.
- Studies of long-term renal function in children following nephrectomy have found abnormalities including microalbuminuria, proteinuria, and a reduced glomerular filtration rate; however, other investigators have found no significant alterations in renal function.
- There is no basis to expect renal deterioration in kidney donors because renal function is well preserved in over 20 years of follow-up after donor nephrectomy.

failure, progresses to WAGR patients who have more severe genitourinary anomalies and high long-term risk of renal failure, and finishes with the Denys-Drash syndrome patients, who have markedly distorted genitourinary development and a high risk of early renal failure.

In summary, it is important that these children who have a solitary functioning kidney have long-term follow-up with measurements of blood pressure, urine protein, serum creatinine, renal clearance, and renal size. These children should be followed until they reach adulthood because they could experience subtle renal deterioration at that time or later in adult life.

Renal Function Following Donor Nephrectomy

Renal outcomes in adults with acquired solitary kidney can be studied in a group of patients undergoing donor nephrectomy. Published reports in these patients show no progressive renal injury up to 20 years after kidney donation.⁵⁸ The Cleveland Clinic Foundation recently reported on the impact of donor nephrectomy on estimates of GFR, urinary protein excretion, and the development of hypertension.⁵⁹ Of the 70 patients followed, representing approximately 39% of the live donor pool between 1963–1975, the mean patient follow-up was 25 years. The average donor age at follow-up was 64 years (range 39–84 years). There was a 72% reduction in the value of the 24-hour urinary creatinine clearance which was not dependent upon age. Serum creatinine and systolic blood pressure were significantly increased, although the values were still within the normal range (less than 140/90 mm Hg). Serum creatinine was higher in males before and after donation, but there were no gender differences in the 24-hour urinary creatinine clearance. There were

no differences in these values based on the age at donation. Values for 24-hour urine creatinine clearance after donation were higher than the expected single GFR for males, and no difference was found for females.

The 24-hour urine protein and albumin excretion after donation were higher in males compared with females after donation, but no differences in values were found based on the age at donation. Proteinuria developed in 13 (19%) and albuminuria developed in 23 of 63 patients (36%). No correlation was found between proteinuria and renal function. There was a correlation between albuminuria and serum creatinine but not creatinine clearance. When the group of patients who developed proteinuria was further evaluated, most were found to have mild proteinuria (less than 0.8 g/24 hr.) but 5 had more significant proteinuria. These patients were also noted to have a median proteinuria value before donation of 0.21 g/24 hr, which was higher than the remainder of the group in the study population. These patients represent a subset population who would be at risk for the development of long-term significant proteinuria following donor nephrectomy.

No donor was hypertensive (blood pressure 140/90 mm Hg or greater or normotensive but managed with antihypertensive medications) at the time of donation. Postoperatively, 31 (48%) were hypertensive, which is comparable to the 54% noted in the National Health and Nutrition Examination Survey for Adults 65–74 years of age.⁶⁰ Although systolic blood pressure increased significantly after donation but was still within the normal range (140 mm Hg or less), there was no change in the diastolic blood pressure. Systolic blood pressure after donation increased in all patients but was higher and in the hypertensive range in donors

over 50 years of age. This is due to the age-related increase in blood pressure observed in the general population. One patient developed glomerulonephritis without long-term renal sequelae. End-stage renal disease developed in two patients, but there was insufficient information to determine its etiology. The authors conclude that there is no basis to expect renal deterioration in kidney donors because renal function is well preserved in over 20 years of follow-up after donor nephrectomy. ■

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